

REMARKS

Claims 1-12, 14-19, 21, 22, and 24-37 were pending in this application. Claims 17-19, 21, 22, and 24-34 are cancelled as drawn to non-elected groups. Applicants reserve the right to pursue the cancelled subject matter in a separate application.

Claims 1-4, 6-12, 14-16 and 35-37 are amended. New claims 38-54 are added. Support for the claim amendments and new claims is discussed below, where necessary. No new matter is introduced by these amendments. Unless specifically stated otherwise, none of these amendments are intended to limit the scope of any claim.

After entry of this amendment **claims 1-12, 14-16 and 35-54 are pending in this application**. Consideration of the pending claims is requested.

Election/Restrictions

Applicants note that the Examiner has made the restriction requirement final. Accordingly, Applicants cancel non-elected claims 17-19, 21, 22, and 24-34 herein.

Claim Rejections under 35 U.S.C. §112, 2nd paragraph:

Claims 1-12, 14-16 and 35-37 have been rejected under 35 U.S.C. §112, 2nd paragraph for allegedly being indefinite for the reasons specified below. Applicants traverse rejection of each of these claims.

Claim 1 is allegedly indefinite in the recitation of the term “components.” Claim 1 has been amended to substitute the phrase “cells or tissue structures” for the phrase “components of interest.” Support for this amendment is found throughout the specification, *e.g.*, at page 1, line 8, at page 11, lines 7-9, and at page 15, lines 12-13, page 22, line 30. In light of this claim 1 amendment, this rejection is moot and Applicants request that it be withdrawn.

Claim 4 is allegedly indefinite in the recitation of the phrase “in the presence of water,” and because allegedly there is insufficient antecedent basis for the phrase. Claim 4 has been

amended to remove the allegedly indefinite phrase. Thus, this rejection is moot, and Applicants request that it be withdrawn.

Claim 6 is allegedly indefinite in the recitation of “capture member.” Claim 6 has been amended to substitute “capture film” for “capture member.” This amendment is supported, *e.g.*, at page 1, line 15, in Figure 1, and at page 4, lines 11-15. In light of this amendment, Applicants request that this rejection be withdrawn.

Claim 12 is said to be indefinite because allegedly “it is unclear what structural and functional cooperative relationship exists [sic] between the primary and secondary antibodies and the tissue.” Claim 12 has been amended to recite that the primary and secondary antibodies are pre-mixed “to form the fluorescent specific binding agent.” This amendment is supported, *e.g.*, at page 14, lines 3-10. The relationship between the fluorescent specific binding agent and the tissue is clear from the claim language.

The Office action also states that “it is unclear how one of the antibodies is fluorescent.” Applicants emphasize that the claim recites “*at least one*” of the primary and secondary antibody is fluorescent. Hence, either one or both of the primary and/or secondary antibody(ies) may be fluorescent. Claim 12 has been further amended to recite that at least one of the primary and/or secondary antibody(ies) is “fluorescently labeled.” This amendment is supported throughout the specification, *e.g.*, at page 9, lines 15-16.

The Office action also refers to claim 9 in this rejection (at page 3, lines 22 and 23), *i.e.*, “[s]ee also deficiency in claim 9.” Claim 9 has been amended to recite a “fluorescently labeled” antibody. This amendment is supported at least by the specification, *e.g.*, at page 9, lines 11-19.

In view of the foregoing amendments, Applicants request that this rejection of claim 12 (and claim 9) be withdrawn.

Claim 35 is alleged to be indefinite because (i) “the preamble of the claim does not correlate with the body of the claim,” (ii) “it is unclear what structural and functional cooperative

relationship exists [sic] between the elements recited in the claim such as the tissue, the target cells, the biological molecule and the fluorescent specific binding agent,” (iii) “it is unclear how the tissue preserves a biological molecule,” and (iv) the term “sufficient” is a relative term, which allegedly is not sufficiently defined as to apprise the ordinarily skilled artisan of the scope of the claim.

Claim 35 is now directed to:

“A method for fluorescently labeling tissue containing one or more cells or other tissues structures while preserving a biological molecule contained in the tissue, comprising:

contacting the tissue with a fluorescent specific binding agent of a concentration to provide selectively labeled cells or other tissue structures against which the fluorescent specific binding agent is directed in less than about five minutes;

wherein the biological molecule in the tissue is preserved after the tissue is contacted with the fluorescent specific binding agent, by labeling the cells or other tissue structures in less than five minutes.”

It is believed that the amendments fully and completely address the alleged indefiniteness of this claim. Applicants request that this rejection of claim 35 be withdrawn.

With particular regard to basis (iv) of this rejection, amended claim 35 no longer recites the allegedly relative term “sufficient.” Thus, this basis of the rejection is moot, and Applicants request that it be withdrawn.

Claim 35 now specifies that the tissue is contacted with fluorescent specific binding agent at “a concentration to provide selectively labeled cells or other tissue structures against which the fluorescent specific binding agent is directed in less than about five minutes.” The specification clearly sets out specific examples of concentrations of fluorescent specific binding agent that provide selective labeling of cells or tissues structures (see, *e.g.*, page 28, lines 5-10; page 29, line 24; page 23, lines 15-16; page 34, line 13; and original claims 10 and 11). Moreover, the specification provides extensive guidance regarding how to determine a concentration of fluorescent specific binding agent to selectively label cells or tissue structures (see, *e.g.*, page 21,

line 23 through page 24, line 20). In light of the thorough teaching of the specification, Applicants respectfully submit that the amended language of claim 35 satisfies 35 U.S.C. §112, ¶2.

Claim Rejections under 35 U.S.C. §102:

Claims 1 and 35 have been rejected under 35 U.S.C. §102(a) as being allegedly anticipated by Fink *et al.* (*Laboratory Investigation*, 80:327-333, March 2000) (“Fink”). Applicants traverse this rejection.

Fink describes protocols for immunohistochemistry and immunofluorescence with total incubation times of approximately 25 to 40 minutes and 10 to 20 minutes, respectively (see, Fink, page 327, “Summary”). The Office action specifically points to page 332 of Fink, which describes a method of immunofluorescence that includes a primary antibody incubation of 3 to 10 minutes, a wash, and a secondary antibody incubation of 3 to 10 minutes. Presumably, this method is one of those immunofluorescence methods described by the authors in the Summary with a total incubation time of 10 to 20 minutes. However, even assuming that the wash step described by Fink was instantaneous (which it could not be) and the two labeling steps took the minimum described time, the labeling procedure described by Fink on page 332 could take *no less than 6 minutes*. Claims 1 and 35 recite, in relevant part, “selectively label[ing] target cells . . . in less than about five minutes.” Thus, Fink does not teach all of the elements of claims 1 and 35 and cannot, therefore, anticipate these claims. Applicants request that this rejection be withdrawn.

Claim Rejections under 35 U.S.C. §103:

Claims 1, 4-6, 9, and 35 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Liotta *et al.*, U.S. 6,251,467, issued June 26, 2001 (“Liotta”), in view of Fink. Applicants traverse this rejection.

The Office action states (at page 6, lines 3-5 of the Office action) that Liotta fails to teach that “the label is fluorescent and that the fluorescent specific binding agent is directed in less than about five minutes.” As discussed above, Fink does not make up this deficiency in Liotta,

because Fink actually describes total incubation times of approximately 25 to 40 minutes and 10 to 20 minutes for immunohistochemistry and immunofluorescence methods, respectively. Thus, Liotta and/or Fink do not teach or suggest all of the elements of the claims, and a *prima facie* case of obviousness has not been established.

As explained in the specification (*e.g.*, Example 3), it had not been known how to identify cells or tissue structures by labeling with solutions of fluorescent specific binding agents while simultaneously preserving biological molecules such as RNA, DNA, lipids, secondary metabolites, and proteins, particularly RNA, DNA, and proteins, and in particular mRNA. For example, the specification shows that exposure to aqueous labeling solutions for more than about five minutes is sufficient to result in an almost total loss of tissue RNA, especially mRNA (see, *e.g.*, Example 2; Figures 4 and 5). Thus, selective labeling of cells or tissue structures in less than about five minutes is an important advance that is not taught or suggested by the prior art. Applicants request that the §103(a) rejection be withdrawn.

Claims 2, 3, 7, 8, 10, 11, 14-16, 36 and 37 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Liotta in view of Fink, and further in view of Rushbrooke *et al.*, U.S. 4,922,092, issued May 1, 1990 (“Rushbrooke”). Applicants traverse this rejection.

As discussed above, Liotta and/or Fink do not teach or suggest “selectively label[ing] target cells . . . in less than about five minutes,” as recited in the claims. Similarly, Rushbrooke does not teach or suggest this limitation. Thus, the cited references (either alone or in combination) fail to teach or suggest all of the elements of the claims, and a *prima facie* case of obviousness has not been established. Applicants request that the rejection be withdrawn.

New Claim 38

Applicants thank the Examiner for indicating that claim 12 would be allowable if rewritten in independent format (at page 8, ¶9 of the Office action). Claim 38 has been added for this purpose. Claim 38 is written in independent form and recites all of the limitations of claims 1 and 12. Applicants note that certain limitations in claim 9 (from which claim 12 depended), *i.e.*, “lectin, protein A, protein G or mixtures thereof” are inapplicable and have not been

included in claim 38. Moreover, claim 38 does not recite the allegedly indefinite terms identified in claims 1, 9, and 12 by the Office action. Applicants request that claim 38 be allowed, for the reasons proposed by the Examiner.

New Claims 39-54

New claims 39-54 have been added to the application; support for these claims is found throughout the specification and the original claims.

These new claims are clearly directed to the elected invention (Group I, method for microdissecting tissue), and so are proper in the current case. In addition, it is believed that each of the claims satisfies the requirements of 35 U.S.C. §112, and is novel and non-obvious in light of the art of record. Applicants therefore request that the Examiner allow these claims.

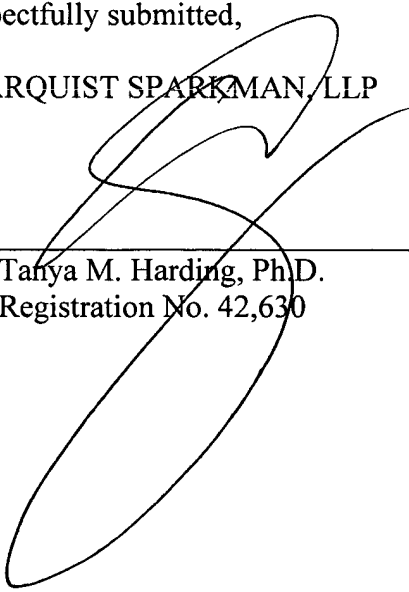
CONCLUSIONS

It is respectfully submitted that the present claims are in a condition for allowance. If any issues remain after entry of this amendment, Applicants hereby expressly request that the Examiner call the undersigned at the telephone number listed below to schedule an interview to discuss the claims.

Respectfully submitted,

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